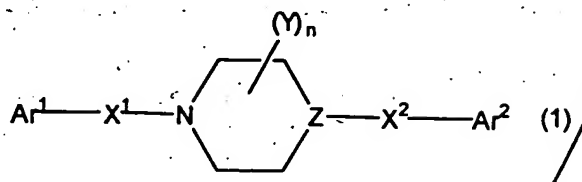
Claims

1. A compound of the formula:



and the pharmaceutically acceptable salts thereof

wherein Ar^1 is indole, benzimidazole, or benzotriazole, optionally substituted with lower alkyl (1-4C), halo, or lower alkoxy (1-4C);

X^1 is CO or an isostere thereof;

Y is optionally substituted alkyl, optionally substituted aryl, or optionally substituted arylalkyl;

n is 0 or 1;

Z is CH or N;

X^2 is CH, CH_2 or an isostere thereof; and

Ar^2 consists of one or two phenyl moieties directly coupled to X^2 and optionally substituted by halo, nitro, alkyl (1-6C), CN or CF_3, or by RCO, COOR, $CONR_2$, NR_2, OR or SR, wherein R is H or alkyl (1-6C) or by phenyl, itself optionally substituted by the foregoing substituents;

with the proviso that if Z is N, X^1 is CO, and Ar^1 is indole, Ar^1 must be coupled to X^1 through the 2-, 5-, 6- or 7-position.

2. The compound of claim 1 wherein n is 0.

3. The compound of claim 1 wherein Z is CH.

4. The compound of claim 3 wherein X^1 is CO.

5. The compound of claim 3 wherein Ar^1 is indole or benzimidazole.

6. The compound of claim 3 wherein n is 0.

7. The compound of claim 3 wherein Ar^1 is coupled to X^1 through the 3, 4, 5 or 6 position.

8. The compound of claim 3 wherein X^2 is CH and Ar^2 consists of two optionally substituted phenyl moieties.

9. The compound of claim 3 wherein X^2 is CH_2 or CO and Ar^2 consists of one optionally substituted phenyl moiety.

10. The compound of claim 3 wherein Ar^2 is phenyl optionally substituted with halo.

11. The compound of claim 1 wherein Ar^1 is coupled to X^1 through its 5-position.

12. The compound of claim 11 wherein X^1 is CO.

13. The compound of claim 11 wherein n is 0.

14. The compound of claim 11 wherein Ar^1 is optionally substituted indole or benimidazole.

15. The compound of claim 11 wherein Ar^1 is optionally substituted indole.

16. The compound of claim 11 wherein X^2 is CH_2 or CO and Ar^2 consists of one optionally substituted phenyl moiety.

17. The compound of claim 11 wherein Ar^2 is phenyl optionally substituted with halo.

18. The compound of claim 1 wherein Ar^1 is optionally substituted indole and Z is CH.

19. The compound of claim 18 wherein Ar^1 is unsubstituted indole.

20. The compound of claim 18 wherein X^1 is CO.

21. The compound of claim 18 wherein n is 0.

22. The compound of claim 18 wherein Ar^1 is coupled to X^1 through the 3, 4, 5 or 6 position.

23. The compound of claim 18 wherein X^2 is CH and Ar^2 consists of two optionally substituted phenyl moieties.

24. The compound of claim 18 wherein X^2 is CH_2 and Ar^2 consists of one optionally substituted phenyl moiety.

25. The compound of claim 18 wherein Ar^2 is phenyl optionally substituted with halo.

26. The compound of claim 1 wherein Ar^1 is optionally substituted benzimidazole.

27. The compound of claim 26 wherein X^1 is CO.

28. The compound of claim 26 wherein n is 0.

29. The compound of claim 26 wherein Ar^1 is coupled to X^1 through the 3, 4, 5 or 6 position.

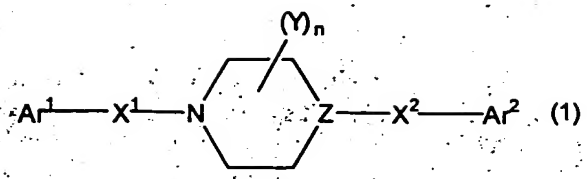
30. The compound of claim 26 wherein X^2 is CH and Ar^2 consists of two optionally substituted phenyl moieties.

31. The compound of claim 26 wherein X^2 is CH_2 and Ar^2 consists of one optionally substituted phenyl moiety.

32. The compound of claim 26 wherein Ar^2 is phenyl optionally substituted with halo.

33. The compound of claim 1 which is 4-benzylpiperidinyl-indole-5-carboxamide or is 4-benzylpiperidinyl-benzimidazole-5-carboxamide.

34. A method to treat a condition characterized by a proinflammation response which method comprises administering to a subject in need of such treatment a compound of the formula



or a pharmaceutically acceptable salt thereof

wherein Ar^1 is indole, benzimidazole, or benzotriazole, optionally substituted with lower alkyl (1-4C), halo, or lower alkoxy (1-4C);

X^1 is CO or an isostere thereof;

Y is optionally substituted alkyl, optionally substituted aryl, or optionally substituted arylalkyl;

n is 0 or 1;

Z is CH or N;

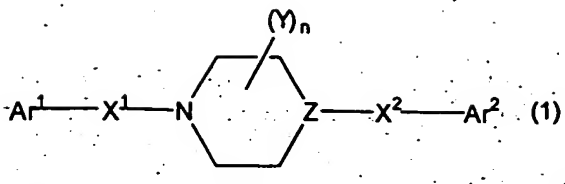
X^2 is CH, CH_2 or an isostere thereof; and

Ar^2 consists of one or two phenyl moieties directly coupled to X^2 and optionally substituted by halo, nitro, alkyl (1-6C), CN or CF_3, or by RCO, COOR, $CONR_2$, NR_2, OR or SR, wherein R is H or alkyl (1-6C) or by phenyl, itself optionally substituted by the foregoing substituents;

with the proviso that if Z is N, X^1 is CO, and Ar^1 is indole, Ar^1 must be coupled to X^1 through the 2-, 5-, 6- or 7-position.

35. The method of claim 34 wherein said condition characterized by inflammation is acute respiratory distress syndrome, asthma, chronic obstructive pulmonary disease, uveitis, IBD, acute renal failure, head trauma, or ischemic/reperfusion injury.

36. A method to treat a heart condition associated with cardiac failure which method comprises administering to a subject in need of such treatment a compound of the formula



or a pharmaceutically acceptable salt thereof

wherein Ar^1 is indole, benzimidazole, or benzotriazole, optionally substituted with lower alkyl (1-4C), halo, or lower alkoxy (1-4C);

X^1 is CO or an isostere thereof;

Y is optionally substituted alkyl, optionally substituted aryl, or optionally substituted arylalkyl;

n is 0 or 1;

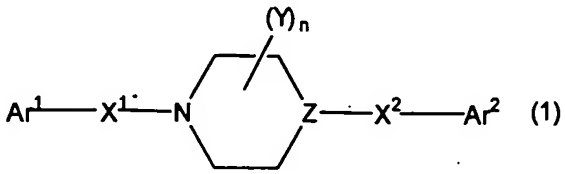
Z is CH or N;

X^2 is CH, CH_2 or an isostere thereof; and

Ar^2 consists of one or two phenyl moieties directly coupled to X^2 and optionally substituted by halo, nitro, alkyl (1-6C), CN or CF_3, or by RCO, COOR, $CONR_2$, NR_2, OR or SR, wherein R is H or alkyl (1-6C) or by phenyl, itself optionally substituted by the foregoing substituents.

37. The method of claim 36 wherein said chronic heart condition is congestive heart failure, cardiomyopathy or myocarditis.

38. A method to prepare a compound of the formula



or a pharmaceutically acceptable salt thereof

wherein Ar^1 is indole, benzimidazole, or benzotriazole, optionally substituted with lower alkyl (1-4C), halo, or lower alkoxy (1-4C);

X^1 is CO or an isostere thereof;

Y is optionally substituted alkyl, optionally substituted aryl, or optionally substituted arylalkyl;

n is 0 or 1;

Z is CH or N;

X^2 is CH, CH_2 or an isostere thereof; and

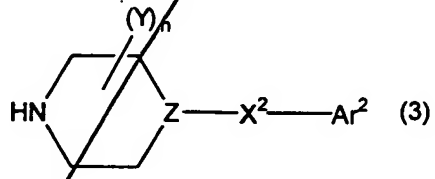
Ar^2 consists of one or two phenyl moieties directly coupled to X^2 and optionally substituted by halo, nitro, alkyl (1-6C), CN or CF_3, or by RCO, COOR, $CONR_2$, NR_2, OR or SR, wherein R is H or alkyl (1-6C) or by phenyl, itself optionally substituted by the foregoing substituents;

which method comprises

(a) reacting a compound of the formula

$$Ar^1\text{-}COOH \qquad (2)$$

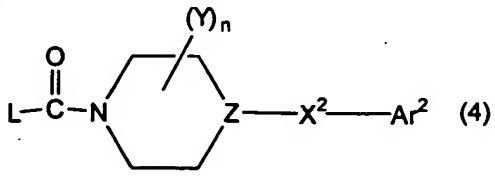
with a compound of the formula



(3)

under conditions wherein the carboxamide is formed; or

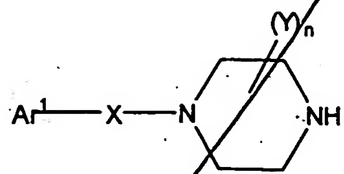
(b) reacting an optionally substituted indole, benzimidazole or benzotriazole with a compound of the formula



(4)

wherein L is leaving group; or

(c) reacting a compound of the formula

 (5)

with a compound of the formula

$$Ar^2\text{-}X^2\text{-}M \qquad (6)$$

wherein M is a halide,

under conditions of mild base.